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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,852	09/22/2000	Per Johan Lundberg	1103326-0686	1116

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WHITE & CASE LLP
PATENT DEPARTMENT
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
TRAN, SUSAN T	
ART UNIT	**PAPER NUMBER**
1615	
MAIL DATE	**DELIVERY MODE**
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/646,852	LUNDBERG ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-10,12-18,20 and 23-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 04/11/07 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-10, 12-18, 20 and 23-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed water-insoluble polymer coating, does not reasonably provide enablement for water-insoluble polymer capable of forming a semipermeable membrane. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Enablement is considered in view of the Wands factors (MPEP § 2164.01 (a)). These include: breadth of the claims; nature of the invention; state of the prior art; amount of direction provided by the inventor; the level of predictability in the art; the existence of working examples; quantity of experimentation needed to make or use the invention based on the content of the disclosure; and relative skill in the art. All of the factors have been considered with regard to the claim, with the most relevant factors discussed below:

The present claims are directed to a delayed release oral dosage form comprising omeprazole core, and a semipermeable membrane coating without an enteric coating.

With respect to the guidance, the present specification fails to teach if all water-insoluble polymers are capable of forming a semipermeable membrane given the multitudes of types of suitable water-insoluble polymers. Examiner notes that example 3 shows the coating membrane consisting of a water-insoluble polymer and talc. However, the example is specific to ethylcellulose, not all water-insoluble polymers. Further, example 3 does not shows that the coating is a semipermeable membrane. Thus, guidance for preparing and using a composition comprising all the possible water-insoluble polymers with omeprazole is not provided in the instant specification. Consequently, a burdensome amount of research would be required by one of ordinary skill in the art to bridge this gap.

As such, the practitioner would turn to trial and error experimentation in order to compose a composition comprising omeprazole with any type of water-insoluble

polymers that capable of forming a semipermeable membrane, without guidance from the specification or the prior art.

The quantity of experimentation: in the present case, there is a substantial gap between a composition comprising the claimed drug and a specific water-insoluble polymer that capable of forming a semipermeable membrane, and one comprising any and all "water-insoluble polymers". As stated above, "water-insoluble polymers" comprise a huge class of compounds and not all of them result in the same property with a given drug. Consequently, a burdensome amount of research would be required by one of ordinary skill in the art to bridge this gap.

The relative skill of those in the art: the skill of one of ordinary skill in the art is very high, e.g., Ph.D. and M.D. level technology.

Claim Rejections - 35 USC § 103

Claims 1, 3, 6-8, 12-18, 20 and 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265.

Nara teaches a controlled release composition comprising a drug-containing core coated with a protective coating layer containing hydrophilic substances (column 6, lines 1-10). Hydrophilic substances include hydroxypropyl cellulose, hydroxypropylmethyl cellulose, methylcellulose, polyvinylpyrrolidone, and polyvinyl alcohol (column 5, lines 1-4). The amount of this protective coating is about 1 to about 15% to the core (ID). Drugs include omeprazole and lansoprazole (column 3, lines 59-60). The drug is mixed

with excipient, such as sucrose or calcium phosphate (osmotic agent); binder; disintegrant, such as, sodium crosslinked carboxymethylcellulose or low-substitutional hydroxypropyl cellulose (swelling agent); and lubricant, including talc (alkaline additive) (column 5, lines 36-52; and examples). The core can be in the form of a granule, fine granule, or inert carrier particles including sucrose (column 5, lines 30-35, and 60-65). The coated core can be prepared in tablet or capsule form for oral administration (column 6, lines 56-65; and claim 7).

Nara does not explicitly teach the addition of a modifying agent in the protective coating composition.

Bergstrand teaches an omeprazole core is coated with a separating layer (protective coating layer) comprising polymer such as ethylcellulose, hydroxypropyl methylcellulose, polyvinylpyrrolidone, methylcellulose, and polyvinyl alcohol (column 7, lines 51-61). Bergstrand further teaches the polymer can be used alone (as a single polymer) (column 7, line 62). The separating layer further comprises plasticizer, and antistatic agents such as talc (column 7, lines 63-65; and examples 1, 3 and 7). Thus, it would have been obvious to one of ordinary skill in the art to modify the protective coating composition of Nara to include additives such as talc in view of the teaching of Bergstrand to obtain the claimed invention, because Bergstrand teaches adding talc to the coating composition to increase the thickness of the layer and thereby strengthen the diffusion barrier, because Bergstrand teaches the separating layer improves the chemical stability of the active substance and the physical properties of the dosage form

(column 8, lines 21-27), because Nara teaches the desirability of using a separating layer to protect the acid sensitive active core.

Regarding the limitation "water-insoluble polymer capable of forming a semipermeable membrane", it is noted that Nara and Bergstrand teach the use of the claimed water-insoluble polymers. Therefore, the burden is shifted to applicant to show that the water-insoluble polymers taught by Nara and Bergstrand do not have the claimed property. This is because identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Claims 30 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. US 5,753,265 and Hodges et al. US 5,225,202.

Nara is relied upon for the reason stated above. Nara does not explicitly teach the amount of alkaline additive present in the core.

Hodges teaches a controlled release pellet comprising acid labile drug in the core, and one or more buffering agents (alkaline additives) (see abstract, and column 3, lines 1-4; lines 15-19). Buffering agents present in the core in an amount ranging from about 1 to about 20% (column 3, lines 34-36). Thus, it would have been obvious to one of ordinary skill in the art to use alkaline additive in an amount taught by Hodges to obtain a stable acid labile composition, because Hodges teaches using buffering agent in an amount of about 1 to about 20% to aid in minimizing drug degradation in the core

due to acid ingress in low pH environments (column 3, lines 6-9), and because Nara teaches a composition with low toxicity and can be safely used in mammals.

It is noted that Nara does not explicitly teach the weight ratio of the modifying agent to water-insoluble substance, as well as the amount of the alkaline additive and swelling agent in the core. However, generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, it would have been obvious to one of ordinary skill in the art to, by routine experimentation determine suitable amount of talc in the core composition as well as in the coating composition, because Nara teaches the release rate of the active ingredient is mainly in the small and large intestine without an enteric coating, while the release rate of the active ingredient is very limited in the stomach (column 1, lines 53-55; and column 7, lines 25-31), and because Nara teaches a coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit release of omeprazole in the stomach, but increases release in the small and large intestine.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al. and, Zentner US 4,795,644 or Lundberg et al. 6,013,281.

Nara is relied upon for the reasons stated above. Nara is silent of the claimed alkaline agent.

Zentner teaches pH-modifying agent includes sodium mono- or di-phosphate (column 8, lines 3-15).

Lundberg teaches alkaline reacting compound includes arginine (column 6, lines 50-55). Thus, it would have been obvious to one of ordinary skill in the art to modify the compositions of Nara using sodium mono- or di-phosphate and arginine compound as an alkaline agent, because the references teach suitable composition for the same active agent, namely, omeprazole, and because Nara teaches the desirability of using an alkaline agent in the composition.

Claims 4, 5 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nara et al. US 6,245,351, in view of Bergstrand et al., and Cotton et al. WO 98/54171.

Nara is relied upon for the reasons stated above. Nara is deficient in the fact that Nara does not specifically teach magnesium salt of omeprazole.

Cotton teaches novel form of S-enantiomer of omeprazole, including S-omeprazole, and more specifically, magnesium salt of S-omeprazole trihydrate (hereafter, the compound) (see abstract, and page 1, lines 4-10). Cotton also teaches

the compound is formulated into oral dosage form, *e.g.*, capsule, tablet, and the like (page 6, lines 15-30). The formulation is effective as a gastric acid secretion inhibitor and is useful as an anti-ulcer agent (page 6, lines 1-14).

Cotton does not explicitly teaches the compound having a crystallinity of more than 70%, however, Cotton teaches that the compound of his invention is highly crystalline, *i.e.*, having a higher crystallinity than any other form of magnesium salt of S-omeprazole in the prior art (page 3, lines 24 through page 4, lines 1-7). Therefore, the burden is shifted to applicant to show the compound taught by Cotton does not have the crystallinity being claimed. It is also noted that Cotton teaches the trihydrate form, *e.g.*, magnesium salt of S-omeprazole "trihydrate". However, applicant claims recite a generic form of magnesium salt of S-omeprazole with the transitional phrase "comprising of" permits any other form, including "trihydrate" taught by Cotton. Thus, it would have been obvious for one of ordinary skill in the art to modify the controlled release composition comprising a drug-containing core coated with a *non-enteric* coating composition using the magnesium salt of S-omeprazole trihydrate in view of the teaching of Cotton, because Cotton teaches the compound of his invention is more stable, easier to handle and store, easier to synthesize in a reproducible manner, because Cotton teaches the compound is most preferred in oral administration formulation, because Nara teaches a non-enteric coated formulation with low toxicity that can be safely used in human. The expected result would be a controlled-release composition comprising omeprazole in the core without enteric coating that can limit

release of omeprazole in the stomach, but increases release in the small and large intestine.

Response to Arguments

Applicant's arguments filed 04/11/07 have been fully considered but they are not persuasive.

Applicant argues that when the water-insoluble substance of Nara is a polymer, *e.g.*, a cellulose ether, an acrylic polymer, etc., Nara's coating composition contains at least two polymers: the water-insoluble polymer and the swellable polymer. Such a two-polymer system does not suggest the single polymer coating composition of the claimed invention. When the water-insoluble substance of Nara is not a polymer, *e.g.*, a hydrogenated oil, wax, etc., Nara does not disclose or suggest that the swellable polymer must be both water-insoluble and capable of forming a semipermeable membrane. The first category, i.e., swellable polymers which do not have any basic groups, is illustrated by HPC, a known film-forming agent. However, HPC is water-soluble. Therefore, when Nara's water-insoluble substance is not a polymer, this first category of swellable polymers as illustrated by HPC does not meet the claim requirement that the single polymer coating composition is water-insoluble and capable of forming a semipermeable membrane. The second category, *i.e.*, swellable polymers having an acidic dissociating group, is illustrated by the following cross-linked acrylic polymers: Carbomer (water soluble); polycarbophil and calcium polycarbophil (incapable of forming a semipermeable membrane); and HIVISWAK carboxyvinyl

polymers (hydrophilic water soluble). Therefore, when Nara's water-insoluble substance is not a polymer, this second category of swellable polymers as illustrated by Carbomer, polycarbophil, calcium polycarbophil and HIVISWAK, does not meet the claim requirement that the single polymeric component of tile single polymer coating composition is water-insoluble and capable of forming a semipermeable membrane.

However, in response to applicant's arguments, applicant's attention is called to column 6, lines 10-10, and column 5, lines 1-5, where Nara teaches a protective coating layer comprises the claimed water-insoluble polymer. Accordingly, the burden is shifted to applicant to show that the water-insoluble polymer taught by Nara is not capable of forming a semipermeable membrane. Further, Nara is now cited in combination with Bergstrand et al. for the specific teaching of a protective coating layer that comprises the claimed components, such as a single polymer and talc.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN TRAN
PRIMARY EXAMINER

Art Unit 1615